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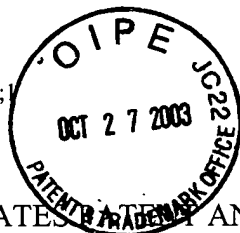
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Tony W. Ho, Gene C. Kopen, William F. Righter, J. Lynn Rutkowski and Joseph Wagner

Application No.: 09/960,244 Group Art Unit: 1651

Filed: September 21, 2001 Examiner: Vera Afremova

Confirmation No.: 4326

Title: Cell Populations Which Co-Express CD49c and CD90

CERTIFICATE OF MAILING OR TRANSMISSION	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, or is being facsimile transmitted to the United States Patent and Trademark Office on:	
10-22-03	<i>Jane Morgan</i>
Date	Signature
JANE	MORGAN
Typed or printed name of person signing certificate	

TRANSMITTAL OF INTERNATIONAL SEARCH REPORT AND INVITATION TO PAY ADDITIONAL FEES CITED IN A RELATED INTERNATIONAL PATENT APPLICATION

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Transmitted herewith is a copy of an International Search Report and an Invitation to Pay Additional Fees (with a Partial International Search Report) cited in a foreign patent office in a related international application. The references cited in the International Search Report and the Invitation to Pay Additional Fees have been previously cited by Applicants and the Patent Office in the above-referenced application.

Applicants believe no fees are due in this matter. Please charge any deficiency in fees to Deposit Account 08-0380.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By *Mary K. Murray*

Mary K. Murray  
Registration No.: 47,813  
Telephone: (978) 341-0036  
Facsimile: (978) 341-0136

Concord, MA 01742-9133

Dated: October 22, 2003



## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

DOCKETED

COPY

To:  
N. SCOTT PIERCE  
HAMILTON, BROOK, SMITH & REYNOLDS, PC  
530 VIRGINIA ROAD, P.O. BOX 9133  
CONCORD, MA 01742-9133

PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Date of Mailing  
(day/month/year) 07 July 2003

Applicant's or agent's file reference

2831.2003003

PAYMENT DUE

within 15 days  
from the above date of mailing

International application No.

PCT/US02/29971

International filing date  
(day/month/year) 20 September 2002 (20.09.2002)

Applicant

NEURONYX, INC.

FOREIGN DOCKETING

## 1. This International Searching Authority

(i) considers that there are 36 (number of) inventions claimed in the international application covered by the claims indicated below/on an extra sheet:  
Please See Continuation Sheet

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below/on an extra sheet:  
Please See Continuation Sheet

- (ii) ☐ has carried out a partial international search (see Annex) ☒ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.: 1-13 and 95
- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid.

## 2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:

\$210.00                      X 35                      = \$7,350.00  
Fee additional per invention      number of additional inventions      total amount of additional fees

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☒ Claim(s) Nos. none have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

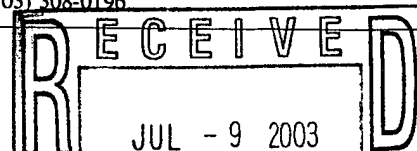
Facsimile No. (703)305-3230

Form PCT/ISA/206 (July 1992)

Authorized officer

Valerie Ball-Harris fw  
Vera Afremova

Telephone No. (703) 308-0196



# INVITATION TO PAY ADDITIONAL FEES

International application No.  
PCT/US02/29971

This International Search Authority has found 36 inventions claimed in the International Application covered by the claims indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-13 and 95 drawn to a first product with a cell population which co-express CD49c, CD90 and telomerase.

Group II, claim(s) 14, drawn to a second product with a cell population which co-express CD49c, CD90 but not CD34 and/or CD45.

Group III, claim(s) 15, drawn to a third product with a cell population which co-express CD49c, CD90 and a trophic factor.

Group IV, claim(s) 16-28, drawn to a 4<sup>th</sup> product with a cell population which co-express CD49c, CD90 but not sialoprotein.

Group V, claim(s) 29-47, 49 and 50, drawn to a first method of making a cell population which co-express CD49c and CD90 based on cell density.

Group VI, claim(s) 48 and 51-62, drawn to a second method of making a cell population which co-express CD49c and CD90 based on cell adherence.

Group VII, claim(s) 63, drawn to a first method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c and CD90.

Group VIII, claim(s) 64, 65 and 96, drawn to a second method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90.

Group IX, claim(s) 66, drawn to a third method of treating human suffering from cardiac condition by administering a cell population which co-express CD49c and CD90.

Group X, claim(s) 67-74, drawn to a 4<sup>th</sup> method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90 and obtained by first method of making.

Group XI, claim(s) 75-79, drawn to a third method of making a committed progenitor cell population which co-express CD49c and CD90.

Group XII, claim(s) 80, drawn to a 5<sup>th</sup> method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c, CD90 and telomerase.

Group XIII, claim(s) 81-89, drawn to a 6<sup>th</sup> method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90 and obtained by third method of making.

Group XIV, claim(s) 90-94, drawn to a 5<sup>th</sup> product with a cell population which co-express CD49c and CD90.

Group XV, claim(s) 96, drawn to a 7<sup>th</sup> method of treating human suffering from neurological condition by administering a cell population which co-express CD49c, CD90 and telomerase.

Group XVI, claim(s) 97, drawn to an 8<sup>th</sup> method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c, CD90 and bone linkage marker.

Group XVII, claim(s) 98, drawn to a 9<sup>th</sup> method of treating human suffering from a neurological condition by administering a cell population which co-express CD49c, CD90 and bone linkage marker.

Group XVIII, claim(s) 99-105 and 155, drawn to a 6<sup>th</sup> product with a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XIX, claim(s) 106 and 107, drawn to a 7<sup>th</sup> product with cell population which co-express CD49c, CD90 and cardiac-related transcription factor but not bone sialoprotein.

Group XX, claim(s) 108 and 158, drawn to an 8<sup>th</sup> product with a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5

Group XXI, claim(s) 109, 156 and 157, drawn to a 9<sup>th</sup> product with a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

# INVITATION TO PAY ADDITIONAL FEES

International application No.  
PCT/US02/29971

Group XXII, claim(s) 110-114 and 121, drawn to a 4<sup>th</sup> method of making a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXIII, claim(s) 115 and 122, drawn to a 5<sup>th</sup> method of making a cell population which co-express CD49c, CD90, cardiac-related transcription factor and telomerase.

Group XXIV, claim(s) 116-119 and 123, drawn to a 6<sup>th</sup> method of making a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXV, claim(s) 124-126, drawn to a 10<sup>th</sup> method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXVI, claim(s) 127, drawn to a 11<sup>th</sup> method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5.

Group XXVII, claim(s) 128, drawn to a 12<sup>th</sup> method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXVIII, claim(s) 129-135, drawn to a 13<sup>th</sup> method of treating a myocardial infarction by administering a cell population cultured at low oxygen condition.

Group XXIX, claim(s) 136-139, drawn to a 14<sup>th</sup> method of treating a myocardial infarction by administering a cell population obtained by fourth method of making.

Group XXX, claim(s) 140 and 141, drawn to a 15<sup>th</sup> method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXXI, claim(s) 142, drawn to a 16<sup>th</sup> method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5.

Group XXXII, claim(s) 143, drawn to a 17<sup>th</sup> method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXXIII, claim(s) 144, drawn to a 18<sup>th</sup> method of treating a congestive heart failure by administering a cell population cultured at low oxygen condition.

Group XXXIV, claim(s) 145-147, drawn to a 7<sup>th</sup> method of making a committed cell population comprising cells which co-express CD49c and CD90 and committed progenitor cells.

Group XXXV, claim(s) 148-153, drawn to a 10<sup>th</sup> product with a cell population which co-express CD49c and CD90 and having specific doubling time when cultured under low oxygen condition.

Group XXXVI, claim(s) 154, drawn to an 11<sup>th</sup> product with a cell population which co-express CD49c and CD90 and having specific doubling time when cultured under low oxygen condition obtained by method.

1. This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:  
The inventions listed as Groups I-XXXVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Claims of the Groups I-XXXVI are directed to more than one of permissible combinations of invention categories such as several different products, several different methods of making different products and several methods of using several products. Moreover, the special technical feature such as cell population co-expressing CD49c and CD90 is known in the prior art. For example: the reference by Ross et al discloses mesothelial cell population co-expressing CD49c and CD90. Thus, the unity of invention is broken.

# COPY

DOCKETED

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
N. SCOTT PIERCE  
HAMILTON, BROOK, SMITH & REYNOLDS, PC  
530 VIRGINIA ROAD, P.O. BOX 9133  
CONCORD, MA 01742-9133

PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 2831.2003003	Date of Mailing (day/month/year)
International application No. PCT/US02/29971	FOR FURTHER ACTION See paragraphs 1 and 4 below
Applicant NEURONYX, INC.	International filing date (day/month/year) 20 September 2002 (20.09.2002)

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

#### Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

**Where?** Directly to the International Bureau of WIPO, 34, chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

#### 4. Reminders

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 bis.1 and 90 bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the PCT Applicant's Guide, Volume II, National Chapters and the WIPO Internet site.

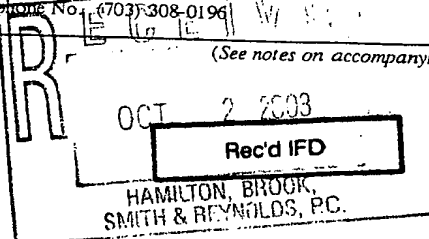
Name and mailing address of the ISA/US  
Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (703)305-3230  
Form PCT/ISA/220 (April 2002)

Authorized officer

Vera Artemova

Telephone No. (703)308-0196

(See notes on accompanying sheet)



# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
N. SCOTT PIERCE  
HAMILTON, BROOK, SMITH & REYNOLDS, PC  
530 VIRGINIA ROAD, P.O. BOX 9133  
CONCORD, MA 01742-9133

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 2831.2003003	Date of Mailing (day/month/year) <b>30 SEP 2003</b>
International application No. PCT/US02/29971	International filing date (day/month/year) 20 September 2002 (20.09.2002)
Applicant NEURONYX, INC.	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

**Where?** Directly to the International Bureau of WIPO, 34, chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 *bis*.1 and 90 *bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer <i>Valerie Bell-Harris</i> Vera Artemova Telephone No. (703) 308-0196
--	---

Form PCT/ISA/220 (April 2002)

(See notes on accompanying sheet)

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 2831.2003003	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US02/29971	International filing date ( <i>day/month/year</i> ) 20 September 2002 (20.09.2002)	(Earliest) Priority Date ( <i>day/month/year</i> ) 21 September 2001 (21.09.2001)
Applicant NEURONYX, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 1 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/29971

## **B x I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## **Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-28 and 95
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

☐  
☒

- The additional search fees were accompanied by the applicant's protest.  
No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/29971

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 5/06, 5/08

US CL : 435/366, 372

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 435/366, 372

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/11011 A2 (FURCHT et al) 15 February 2001 (15.02.2001), page 8, lines 23-30; page 24, line 20; page 26, line 13, page 73, line 13.	1-28, 95
Y	PITTINGER et al. Multilineage Potential of Adult Human Mesenchymal Stem Cells. Science. 2 April 1999, Vol 284, pages 143-147, especially page 144, columns 1 and 2.	1-28, 95
Y	US 5,837,539 A (CAPLAN et al) 17 November 1998 (17.11.1998), table 5 and column 40, line 30.	1-28, 95
Y	COOPER et al. Incipient Analysis of Mesenchymal Stem-cell-derived Osteogenesis. J. Dent. Res. 2001, Vol 80, No. 1, pages 314-320, especially abstract.	16
Y	BOS et al. P21cip1 Rescues Human Mesenchymal Stem Cells from Apoptosis Induced by Low-Density Culture. Cell Tissue Res. 1998, Vol 293, pages 464-470, especially	8,23
Y	GARTEL et al. Transcriptional Regulation of the p21(waf1/cip1) Gene. Experimental Cell Research. 1999, Vol 246, pages 280-289, especially page 281.	8,23

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

13 September 2003 (13.09.2003)

Date of mailing of the international search report

30 SEP 2003

Name and mailing address of the ISA/US

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

Vera Afremova

Telephone No. (703) 308-0196

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

- Group I, claim(s) 1-13 and 95 drawn to a first product with a cell population which co-express CD49c, CD90 and telomerase.
- Group II, claim(s) 14, drawn to a second product with a cell population which co-express CD49c, CD90 but not CD34 and/or CD45.
- Group III, claim(s) 15, drawn to a third product with a cell population which co-express CD49c, CD90 and a trophic factor.
- Group IV, claim(s) 16-28, drawn to a 4<sup>th</sup> product with a cell population which co-express CD49c, CD90 but not sialoprotein.
- Group V, claim(s) 29-47, 49 and 50, drawn to a first method of making a cell population which co-express CD49c and CD90 based on cell density.
- Group VI, claim(s) 48 and 51-62, drawn to a second method of making a cell population which co-express CD49c and CD90 based on cell adherence.
- Group VII, claim(s) 63, drawn to a first method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c and CD90.
- Group VIII, claim(s) 64, 65 and 96, drawn to a second method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90.
- Group IX, claim(s) 66, drawn to a third method of treating human suffering from cardiac condition by administering a cell population which co-express CD49c and CD90.
- Group X, claim(s) 67-74, drawn to a 4<sup>th</sup> method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90 and obtained by first method of making.
- Group XI, claim(s) 75-79, drawn to a third method of making a committed progenitor cell population which co-express CD49c and CD90.
- Group XII, claim(s) 80, drawn to a 5<sup>th</sup> method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c, CD90 and telomerase.
- Group XIII, claim(s) 81-89, drawn to a 6<sup>th</sup> method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90 and obtained by third method of making.
- Group XIV, claim(s) 90-94, drawn to a 5<sup>th</sup> product with a cell population which co-express CD49c and CD90.
- Group XV, claim(s) 96, drawn to a 7<sup>th</sup> method of treating human suffering from neurological condition by administering a cell population which co-express CD49c, CD90 and telomerase.
- Group XVI, claim(s) 97, drawn to an 8<sup>th</sup> method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c, CD90 and bone linkage marker.
- Group XVII, claim(s) 98, drawn to a 9<sup>th</sup> method of treating human suffering from a neurological condition by administering a cell population which co-express CD49c, CD90 and bone linkage marker.

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Group XVIII, claim(s) 99-105 and 155, drawn to a 6<sup>th</sup> product with a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XIX, claim(s) 106 and 107, drawn to a 7<sup>th</sup> product with cell population which co-express CD49c, CD90 and cardiac-related transcription factor but not bone sialoprotein.

Group XX, claim(s) 108 and 158, drawn to an 8<sup>th</sup> product with a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5

Group XXI, claim(s) 109, 156 and 157, drawn to a 9<sup>th</sup> product with a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXII, claim(s) 110-114 and 121, drawn to a 4<sup>th</sup> method of making a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXIII, claim(s) 115 and 122, drawn to a 5<sup>th</sup> method of making a cell population which co-express CD49c, CD90, cardiac-related transcription factor and telomerase.

Group XXIV, claim(s) 116-119 and 123, drawn to a 6<sup>th</sup> method of making a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXV, claim(s) 124-126, drawn to a 10<sup>th</sup> method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXVI, claim(s) 127, drawn to a 11<sup>th</sup> method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5.

Group XXVII, claim(s) 128, drawn to a 12<sup>th</sup> method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXVIII, claim(s) 129-135, drawn to a 13<sup>th</sup> method of treating a myocardial infarction by administering a cell population cultured at low oxygen condition.

Group XXIX, claim(s) 136-139, drawn to a 14<sup>th</sup> method of treating a myocardial infarction by administering a cell population obtained by fourth method of making.

Group XXX, claim(s) 140 and 141, drawn to a 15<sup>th</sup> method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXXI, claim(s) 142, drawn to a 16<sup>th</sup> method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5.

Group XXXII, claim(s) 143, drawn to a 17<sup>th</sup> method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXXIII, claim(s) 144, drawn to a 18<sup>th</sup> method of treating a congestive heart failure by administering a cell population cultured at low oxygen condition.

Group XXXIV, claim(s) 145-147, drawn to a 7<sup>th</sup> method of making a committed cell population comprising cells which co-express CD49c and CD90 and committed progenitor cells.

Group XXXV, claim(s) 148-153, drawn to a 10<sup>th</sup> product with a cell population which co-express CD49c and CD90 and having specific doubling time when cultured under low oxygen condition.

Group XXXVI, claim(s) 154, drawn to an 11<sup>th</sup> product with a cell population which co-express CD49c and CD90 and having specific doubling time when cultured under low oxygen condition obtained by method.

The inventions listed as Groups I-XXXVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Claims of the Groups I-XXXVI are directed to more than one of permissible combinations of invention categories such as several different products, several different methods of making different products and several methods of using several products. Moreover,

## INTERNATIONAL SEARCH REPORT

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the special technical feature such as cell population co-expressing CD49c and CD90 is known in the prior art. For example: the reference by Ross et al discloses mesothelial cell population co-expressing CD49c and CD90. Thus, the unity of invention is broken.

### **Continuation of B. FIELDS SEARCHED Item 3:**

WEST USPT, DWPI; STN MEDLINE, BIOSIS

search terms: bone marrow, CD49c, CD90, CD34, CD45, telomerase, doubling time, differentiation, bone sialoprotein, trophic factor, p53, p21

# UNITED STATES RECEIVING OFFICE (RO/US) FEE CODING AND RECORDING SHEET

☐ ADD'L SHEETS

## IDENTIFICATION OF THE INTERNATIONAL APPLICATION

INTERNATIONAL APPLICATION NUMBER

PCT/US02/29971

INTERNATIONAL FILING DATE

20.09.2002

APPLICANT (Name)

NEURON4X, INC.

## PAYMENTS

## REFUNDS

Payment on Filing		Deposit Account	Deposit Account	To Deposit Account	To Deposit Account
		08 0380			
Deposit Account		DATE: 22.08.2003	DATE:	DATE:	DATE:
<input type="checkbox"/> CASH/CHECK		<input checked="" type="checkbox"/> CASH/CHECK	<input type="checkbox"/> CASH/CHECK	<input type="checkbox"/> BY CHECK	<input type="checkbox"/> BY CHECK
160		1604 \$840.00			
151					
153					
800					
801					
802					
892					
Total Paid:		Total Paid: \$840.00	Total Paid:	Total Refunded:	Total Refunded:
States Included for 892:		892:	892:		
States Included for 893:		893:	893:		

Date Mailed:

RO/US Authorization

RO/US Authorization

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RO/US Authorization

RO/US Authorization

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**CHAPTER I**  
**PCT TELEPHONE MEMORANDUM**  
**FOR**  
**LACK OF UNITY OF INVENTION**

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PCT No.: PCT/US02/29971

Examiner: Vera Afremova

Attorney spoken to: Scott Pierce

Date of call: 22 August 2003

☒ Amount of payment approved: \$840.00

☒ Deposit account number to be charged: 08-0380

☐ Attorney elected to pay for ALL additional inventions

☒ Attorney elected to pay only for the additional inventions covered by

☒ Group(s): I, II, III and IV

-- encompassing --

☐ Claim(s): 1-28 and 95

☐ Attorney elected NOT to pay for any additional inventions, therefore, only the first claimed invention (Group I) covered by Claim(s) \_\_\_\_\_ has been searched.

☐ Attorney was orally advised that there is no right to protest for any group not paid for.

☐ Attorney was orally advised that any protest must be filed no later than 15 days from the mailing of the Search Report (PCT/ISA/210).

**Time Limit For Filing A Protest**

Applicant is hereby given 15 days from the mailing date of this Search Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 40.2, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

**Detailed Reasons For Holding Lack of Unity of Invention:**

*Note: A copy of this form must be attached to the Search Report.*

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**ATTACHMENT TO CHAPTER I PCT TELEPHONE MEMORANDUM  
FOR  
LACK OF UNITY OF INVENTION**

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This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-13 and 95 drawn to a first product with a cell population which co-express CD49c, CD90 and telomerase.

Group II, claim(s) 14, drawn to a second product with a cell population which co-express CD49c, CD90 but not CD34 and/or CD45.

Group III, claim(s) 15, drawn to a third product with a cell population which co-express CD49c, CD90 and a trophic factor.

Group IV, claim(s) 16-28, drawn to a 4th product with a cell population which co-express CD49c, CD90 but not sialoprotein.

Group V, claim(s) 29-47, 49 and 50, drawn to a first method of making a cell population which co-express CD49c and CD90 based on cell density.

Group VI, claim(s) 48 and 51-62, drawn to a second method of making a cell population which co-express CD49c and CD90 based on cell adherence.

Group VII, claim(s) 63, drawn to a first method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c and CD90.

Group VIII, claim(s) 64, 65 and 96, drawn to a second method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90.

Group IX, claim(s) 66, drawn to a third method of treating human suffering from cardiac condition by administering a cell population which co-express CD49c and CD90.

Group X, claim(s) 67-74, drawn to a 4th method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90 and obtained by first method of making.

Group XI, claim(s) 75-79, drawn to a third method of making a committed progenitor cell population which co-express CD49c and CD90.

Group XII, claim(s) 80, drawn to a 5th method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c, CD90 and telomerase.

Group XIII, claim(s) 81-89, drawn to a 6th method of treating human suffering from neurological condition by administering a cell population which co-express CD49c and CD90 and obtained by third method of making.

Group XIV, claim(s) 90-94, drawn to a 5th product with a cell population which co-express CD49c and CD90.

*Note: A copy of this form must be attached to the Search Report.*

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Group XV, claim(s) 96, drawn to a 7th method of treating human suffering from neurological condition by administering a cell population which co-express CD49c, CD90 and telomerase.

Group XVI, claim(s) 97, drawn to an 8th method of treating human suffering from a degenerative or acute injured condition by administering a cell population which co-express CD49c, CD90 and bone linkage marker.

Group XVII, claim(s) 98, drawn to a 9th method of treating human suffering from a neurological condition by administering a cell population which co-express CD49c, CD90 and bone linkage marker.

Group XVIII, claim(s) 99-105 and 155, drawn to a 6th product with a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XIX, claim(s) 106 and 107, drawn to a 7th product with cell population which co-express CD49c, CD90 and cardiac-related transcription factor but not bone sialoprotein.

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Group XXI, claim(s) 109, 156 and 157, drawn to a 9th product with a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXII, claim(s) 110-114 and 121, drawn to a 4th method of making a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXIII, claim(s) 115 and 122, drawn to a 5th method of making a cell population which co-express CD49c, CD90, cardiac-related transcription factor and telomerase.

Group XXIV, claim(s) 116-119 and 123, drawn to a 6th method of making a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXV, claim(s) 124-126, drawn to a 10th method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXVI, claim(s) 127, drawn to a 11th method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5.

Group XXVII, claim(s) 128, drawn to a 12th method of treating a myocardial infarction by administering a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXVIII, claim(s) 129-135, drawn to a 13th method of treating a myocardial infarction by administering a cell population cultured at low oxygen condition.

Group XXIX, claim(s) 136-139, drawn to a 14th method of treating a myocardial infarction by administering a cell population obtained by fourth method of making.

Group XXX, claim(s) 140 and 141, drawn to a 15th method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90 and cardiac-related transcription factor.

Group XXXI, claim(s) 142, drawn to a 16th method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90, GATA4, Irx4 and Nkx2.5.

Group XXXII, claim(s) 143, drawn to a 17th method of treating a congestive heart failure by administering a cell population which co-express CD49c, CD90, GATA4, Irx4, Nkx2.5 and telomerase.

Group XXXIII, claim(s) 144, drawn to a 18th method of treating a congestive heart failure by administering a cell population cultured at low oxygen condition.

Group XXXIV, claim(s) 145-147, drawn to a 7th method of making a committed cell population comprising cells which co-express CD49c and CD90 and committed progenitor cells.

*Note: A copy of this form must be attached to the Search Report.*

Group XXXV, claim(s) 148-153, drawn to a 10th product with a cell population which co-express CD49c and CD90 and having specific doubling time when cultured under low oxygen condition.

Group XXXVI, claim(s) 154, drawn to an 11th product with a cell population which co-express CD49c and CD90 and having specific doubling time when cultured under low oxygen condition obtained by method.

The inventions listed as Groups I-XXXVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Claims of the Groups I-XXXVI are directed to more than one of permissible combinations of invention categories such as several different products, several different methods of making different products and several methods of using several products. Moreover, the special technical feature such as cell population co-expressing CD49c and CD90 is known in the prior art. For example: the reference by Ross et al discloses mesothelial cell population co-expressing CD49c and CD90. Thus, the unity of invention is broken.

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*Note: A copy of this form must be attached to the Search Report.*

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

**What parts of the international application may be amended ?**

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

**When ?** Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments ?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How ?** Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

**What documents must/may accompany the amendments ?**

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.